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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,654	01/29/2001	Tsvee Lapidot	LAPIDO2	2645
1444	7590	06/15/2004	EXAMINER	
BROWDY AND NEIMARK, P.L.L.C. 624 NINTH STREET, NW SUITE 300 WASHINGTON, DC 20001-5303			WEHBE, ANNE MARIE SABRINA	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 06/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

317.

## Office Action Summary

Application No.

09/744,654

Applicant(s)

LAPIDOT ET AL.

Examiner

Anne Marie S. Wehbe

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 29 March 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 15-21, 23-27, 33, 48, 49 and 117-128 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 15-21, 23-27, 33, 48-49, 117-122, and 127-128 is/are rejected.
- 7) ☒ Claim(s) 123-126 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/29/04 has been entered. Applicant's amendment and response filed concurrently with the RCE request have also been entered. Claims 1, 3-5, 10-14, and 53-116 have now been canceled. New claims 117-128 have been entered. Claims 15-21, 23-27, 33, 48-49, and 117-128 are currently pending and under examination. An action on the merits follows.

Those sections of Title 35, not included in this office action can be found in the previous office action.

### ***Claim Rejections - 35 USC § 102***

The rejection of claims 80-81, 83-94, 96-106, 108-116 under 35 U.S.C. 102(a) as being anticipated by Viardot et al. (1997) Blood, Vol. 10 Suppl. 1 part 1, page 478. is withdrawn in view of applicant's cancellation of the claims.

The rejection of claims 1, 3-14, 53-64, and 80-116 under 35 U.S.C. 102(a) as being anticipated by Mohle et al. (1998), Blood, Vol. 91, No. 12, 4523-4530, is withdrawn in view of applicant's cancellation of the claims.

***Claim Rejections - 35 USC § 103***

The rejection of previously pending claims 15-21, 23-27, 33, 48-49, and 65-79 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,541,103, 7/30/96, hereafter referred to as Kanz et al. in view of Mohle et al. (1998), Blood, Vol. 91, No. 12, 4523-4530, is maintained over original, amended, or new claims 15-21, 23-27, 33, 48-49, 117-122, and 127-128.

Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant claims methods of increasing the population of human hematopoietic stem cells for use in clinical transplantation comprising up-regulating surface CXCR4 expression and sorting out those CXCR4 stem cells that migrate in response to SDF-1. The applicant further claims said methods wherein CXCR4 is up-regulated by stimulation with cytokines such as IL-6 and SCF, or stromal cells, or stromal cells and a mixture of SCF and IL-6. The applicant further claims methods of screening for CXCR4 stem cells suitable for transplantation comprising the stimulation of CXCR4 stem cells with IL-6 and SCF followed by sorting of the cells for SDF-1 responsiveness by carrying out an in vitro transmigration assay across a mechanical barrier of cells wherein the cells to be sorted are the cells which transmigrate in response to SDF-1.

Previous office actions have noted that the intended use of the instant methods for preparing cells

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“for clinical transplantation” recited in the preamble does not constitute a step in the methods as claimed. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure or composition, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. In re Hirao , 535 F.2d 67, 190 USPQ 15 (CCPA 1976); Kropa v. Robie , 88 USPQ 478, 481 (CCPA 1951).

The applicant reiterates their argument that Kanz et al. teaches that treatment of human peripheral blood CD34+ cells with IL-6 and SCF-1 results in expansion of the cells, whereas the instant invention involves increasing the number of cells in a population that express CXCR4 without expansion. In response to applicant's argument that Kanz fails to show certain features of applicant's invention, it is noted that the features upon which applicant relies, i.e., upregulation of CXCR4 without cell expansion, are not recited in the rejected claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Furthermore, the claims as written recite methods of “increasing the population of hematopoietic CXCR4 + stem cells”. Expansion of a cell population by definition increases the overall number of cells including all subpopulations of particular cell types. Thus, treatment of CD34+ cell populations with IL-6 and SCF-1 as taught by Kanz increases the number of CD34+ stem cell which includes CD34+ CXCR4+ stem cells. Therefore, the population of CXCR4+ stem cells is increases, which meets the claim limitation. In addition, Mohle et al. has been cited for teaching and providing motivation for sorting out CXCR4+ stem cells. The resulting population of cells after

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expansion according to Kanz et al. and sorting according to Mohle et al. would thus be not only increased in number but enriched.

The applicant further argues that *prima facie* obviousness can be overcome by a showing of unexpected results, citing MPEP 716.02. The office agrees that a proper showing of unexpected results commensurate in scope with the pending claims can overcome a rejection under 35 U.S.C. 103. However, the applicants have not met the requirements for establishing “unexpected results” regarding the methods as claimed as set forth in MPEP 716.02.

Regarding allegations of “unexpected results”, the MPEP states that the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716,718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results. MPEP 716.01(c). Therefore, applicant’s arguments regarding “unexpected results” are not compelling in the absence of evidence in the form of a declaration or affidavit.

Furthermore, the MPEP clearly states that any showing of “unexpected results” must be commensurate in scope with the claims as written. MPEP 716.02(d). As noted above the claims recite increasing a population of CXCR4+ stem cells and does not recite increasing the number of CXCR4+ stem cells without expansions. Further, the “unexpected finding” in Examples 3 and 4 referred to by the applicants resulted from stimulation of CD34+ cells with SCF for less than 5 days. Only claims 20 and 119 are limited to stimulation with SCF and do not contain any time limitation on exposure of the cells to SCF. There is no evidence of record that any other “agent” suitable for converting CXCR4 -/low cells to CXCR4+ cells encompassed by the claims would have the same effect as SCF. Thus, the results of examples 3 and 4 in the specification are not

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commensurate in scope with the claims as written and cannot be relied upon to overcome the instant rejection.

***Claim Rejections - 35 USC § 112***

The rejection of claims 1, 3-5, 10-14, 53-64, and 80-104 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of applicant's cancellation of the claims.

***Claim Objections***

Claims 123-126 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Amy Nelson, can be reached at (571) 272-0804. For all official communications, the technology center fax number is (703) 872-9306. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737.

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Dr. A.M.S. Wehbé

**ANNE M. WEHBE' PH.D**  
**PRIMARY EXAMINER**

A handwritten signature in black ink, appearing to read 'Anne M. Wehbé', with a long horizontal line extending from the end of the signature.